



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/US99/01619 (22) International Filing Date: 28 January 1999 (28.01.99) (30) Priority Data: 60/072,910 28 January 1998 (28.01.98) US 60/075,954 24 February 1998 (24.02.98) US 60/080,114 31 March 1998 (31.03.98) US 60/080,515 3 April 1998 (03.04.98) US 60/080,666 3 April 1998 (03.04.98) US (71) Applicants (for all designated States except US): CHIRON CORPORATION [US/US]; 4560 Horton Street, Emeryville, CA 94608 (US). HYSEQ INC. [US/US]; 675 Almanor Avenue, Sunnyvale, CA 94086 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): WILLIAMS, Lewis, T. [US/US]; 3 Miroflores, Tiburon, CA 94920 (US). ESCOBEDO, Jaime [CL/US]; 1470 Lavoma Road, Alamo, CA 94507 (US). INNIS, Michael, A. [US/US]; 315 Constance Place, Moraga, CA 94556 (US). GARCIA, Pablo, Dominguez [CL/US]; 882 Chenery Street, San Francisco, CA 94131 (US). SUDDUTH-KLINGER, Julie [US/US]; 280 Lexington Road, Kensington, CA 94707 (US). REINHARD, Christoph [DE/US]; 1633 Clinton Avenue, Alameda, CA 94501 (US).		GIESE, Klaus [DE/US]; 1009 Carolina Street, San Francisco, CA 94107 (US). RANDAZZO, Filippo [US/US]; 6363 Christie Avenue #2511, Emeryville, CA 94608 (US). KENNEDY, Giulia, C. [US/US]; 360 Castenada Avenue, San Francisco, CA 94116 (US). POT, David [CA/US]; 1565 5th Avenue #102, San Francisco, CA 94112 (US). KASSAM, Altaf [US/US]; 394 49th Street, Oakland, CA 94609 (US). LAMSON, George [US/US]; 232 Sandringham Drive, Moraga, CA 94556 (US). DRMANAC, Radoje [YU/US]; 850 East Greenwich Place, Palo Alto, CA 94303 (US). CRKVENJAKOV, Radomir [YU/US]; 762 Haverhill Drive, Sunnyvale, CA 94068 (US). DICKSON, Mark [US/US]; 1411 Gabilan Drive #B, Hollister, CA 95025 (US). DRMANAC, Snezana [YU/US]; 850 East Greenwich Place, Palo Alto, CA 94303 (US). LABAT, Ivan [YU/US]; 140 Acalanes Drive, Sunnyvale, CA 94086 (US). LESHKOWITZ, Dena [US/US]; 678 Durshire Way, Sunnyvale, CA 94087 (US). KITA, David [US/US]; 899 Bounty Drive, Foster City, CA 94404 (US). GARCIA, Veronica [ES/US]; 911 Shell Boulevard #102-0, Foster City, CA 96606 (US). JONES, William, Lee [US/US]; 4290 Albany Drive #P-146, San Jose, CA 95129 (US). STACHE-CRAIN, Birjit [DE/US]; 345 South Mary Avenue, Sunnyvale, CA 94086 (US). (74) Agent: BLACKBURN, Robert, P.; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 23 December 1999 (23.12.99)
(54) Title: HUMAN GENES AND GENE EXPRESSION PRODUCTS II (57) Abstract This invention relates to novel human polynucleotides and variants thereof, their encoded polypeptides and variants thereof, to genes corresponding to these polynucleotides and to proteins expressed by the genes. The invention also relates to diagnostic and therapeutic agents employing such novel human polynucleotides, their corresponding genes or gene products, e.g., these genes and proteins, including probes, antisense constructs, and antibodies.		

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/01619

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/12 C07K14/47 C07K16/18 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C07K C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CARMECI ET AL: "Identification of a gene (GPR30) with homolgy to the G-protein -coupled receptor superfamily associated with estrogen receptor expression in breast cancer" GENOMICS, vol. 45, no. 3, 1 November 1997 (1997-11-01), pages 607-617 17, XP002099963 see page 608, left-hand column, paragraph 3 abstract --- -/--	1-8



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
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- *O* document referring to an oral disclosure, use, exhibition or other means
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- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

2 July 1999

Date of mailing of the international search report

08.11.99

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/01619

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	YEATMAN ET AL: "Identification of genetic alterations associated with the process of human experimental colon cancer liver metastasis in the nude mouse" CLINICAL & EXPERIMENTAL METASTASIS, vol. 14, no. 3, May 1996 (1996-05), pages 246-252 252, XP002099961 abstract ---	1-8
X	YEATMAN T ET AL: "Identification of a differentially-expressed message associated with colon cancer liver metastasis using an improved method of differential display" NUCLEIC ACIDS RESEARCH, vol. 23, no. 19, 1995, pages 4007-4008, XP002099962 the whole document ---	1-8
A	RADINSKY ET AL: "Level and function of epidermal growth factor receptor predict the metastatic potential of human colon carcinoma cells" CLINICAL CANCER RESEARCH, vol. 1, no. 1, January 1995 (1995-01), pages 19-31 31, XP002099964 the whole document ---	
A	BALDI ET AL: "Differential expression of the retinoblastoma gene family members pRb/p105, p107, and pRb2/p130 in lung cancer" CLINICAL CANCER RESEARCH, vol. 2, no. 2, July 1996 (1996-07), pages 1239-1245 45, XP002099965 the whole document ---	
A	OKAMURA K ET AL: "Endogenous basic fibroblast growth factor-dependent induction of collagenase and interleukin-6 in tumor necrosis factor-treated human microvascular endothelial cells" JOURNAL OF BIOLOGICAL CHEMISTRY., vol. 266, no. 29, 15 October 1991 (1991-10-15), pages 19162-19165, XP002108129 figure 5 -----	

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/01619

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION SHEET
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see invention 1.

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Invention 1: claims 1-8

A library of polynucleotides comprising the sequence information of at least one of the sequences 1-3544, 3546-4510, 4512-4725, 4727-4748 and 4750-5252.

2. Invention 2: claims 9, 11-14 all partially

The isolated nucleic acid with SeqIdNo:1, sequences with at least 90% sequence identity therewith and degenerate variants thereof, host comprising said nucleic acid, peptide encoded by said nucleic acid, antibody against said protein, vector comprising said nucleic acid.

3. Inventions 3-5253: claims 9-21, all partially, as far as applicable

As invention 2, and, when applicable, a method for detecting the differential expression of said nucleic acid, but limited respectively to the SeqIdNo:2-5252.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

In view of the large number of libraries, which are defined by the general definition in the independent claim 1, the search had to be restricted for economic reasons. The search was limited to the libraries for which data was given in the description, or libraries derived from cell lines mentioned in table 4 of the description, and to the general idea underlying the application (see Guidelines, Part B, Chapter III, paragraph 3.6.).